Department of Zoology
Indiana University
Bloomington, Indiana
January 4, 1951

Dr. J. Lederberg
Department of Genetics
University of Wisconsin
Madison, Wisconsin

Dear Dr. Lederberg,

I will complete my doctoral research in Dr. Sonneborn's laboratory in June, 1951, and am applying for a Merck Postdoctoral Fellowship for the following academic year. The purpose of this letter is to determine whether or not you and Dr. Irwin (to whom a similar letter has been sent) would be willing and/or in a position to sponsor the program of work I have in mind.

My main interest lies in developmental problems; the basic goal of my research at Indiana has been (in common with that of Dr. Sonneborn's research) the elucidation of the mechanisms determining antigenic type in Paramecium. The program I propose to pursue at Wisconsin is essentially an immunogenetic study of E.coli, strain K-12, with especial emphasis on the possible discovery of non-Mendelian mechanisms determining serological characters similar to (or different from) those operative in Paramecium.

It would be foolish for me to attempt to propose, at this time, elaborate plans of attack, but the essential rationale is as follows: Obtain serologically distinct cultures of K-12 (Does sufficient heterogeneity exist?), each marked with biochemical deficiencies. "Mate" these and examine resulting prototrophs for serotype. If the distribution of specificities among the prototrophs is random or conforms to no linkage pattern, the choice between specificities is determined either by genes on another chromosome or by a "cytoplasmic" mechanism. Providing the first step is feasible, a choice between these two alternatives could be made on the basis of further experiments. If it is demonstrated that the cytoplasm is involved, experiments could be designed to determine the extent of gene-independence of these cytoplasmic determiners -either by mating to (genetically different?) strains other than K-12 (if such is now possible) or by attempting to induce gene mutations affecting specificity. If, on the other hand, the distribution of specificities following "mating" is not random and an orthodox genic basis is indicated, another set of interesting lines of approach exist -e.g. analysis of antiserum-induced (?) changes in serotype, or analysis of the effects of environmental variation upon gene action. Perhaps a better approach to the whole problem would be through an examination of the offspring of isolated diploid cells.

The possibilities of such a study are so intrigueing to me that I'm afraid I have overlooked certain prohibitive technical difficulties which have prevented its being undertaken earlier. Regardless of your decision concerning my coming to Wisconsin, I would appreciate any general criticism of the plan.

Since my present problem is an immunogenetic one and since I have had at least rudimentary training in bacteriological technique I believe my preparation to be adequate, although ofcourse one of my motives in working at Wisconsin would be the opportunity of learning new techniques in both fields. As you know, the deadline for Merck applications is January 15, but I believe there is time for you to obtain any additional information you might want -either from Dr. Sonneborn or myself.

Sincerely,

Palmer D. Skaar

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